Lec.7 medical mycology **Dr. Hamzia Ali**

Coccidioidomycosis (Valley fever **)**

Coccidioidomycosis is initially, a respiratory infection, resulting from the inhalation of conidia, that typically resolves rapidly leaving the patient with a strong specific immunity to re-infection. However, in some individuals the disease may progress to a chronic pulmonary condition or to a systemic disease involving the meninges, bones, joints and subcutaneous and cutaneous tissues. *Coccidioides immitis* is a soil inhabiting fungus endemic in south-western U.S.A., northern Mexico and various centers in South America. Several cases have now been diagnosed in Australia, all in patients with a history of travel to endemic areas.

Clinical manifestations:

60% of individuals suffer a benign and transient chest infection that does not require medical attention. Of the 40% who develop symptoms, most will have an acute febrile "flu-like" illness starting 7-28 days (average 10-16 days) after exposure and most patients will recover completely.

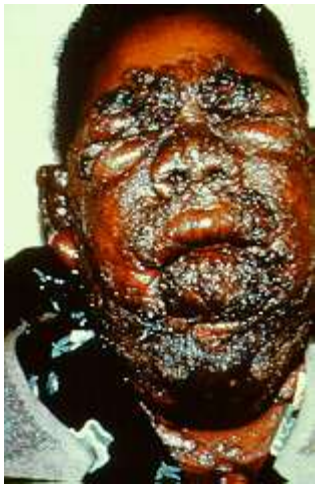
Signs and symptoms

Symptomatic infection (40% of cases) usually presents as an influenza-like illness with fever, cough, headaches, rash, myalgia (muscle pain), and arthralgia (joint pain). The rash is maculopapular. Erythema nodosum on lower extremities, and erythema can occur predominantly in women.

Types

After Coccidioides infection, Coccidioidomycosis begins with Valley fever, which is its initial acute form. If left untreated, it can progress to chronic and then to disseminated Coccidioidomycosis.] Therefore, Coccidioidomycosis may be divided into the following types:

- Acute coccidioidomycosis, sometimes described in literature as primary pulmonary coccidioidomycosis
- Chronic coccidioidomycosis
- Disseminated Coccidioidomycosis, which includes primary cutaneous coccidioidomycosis



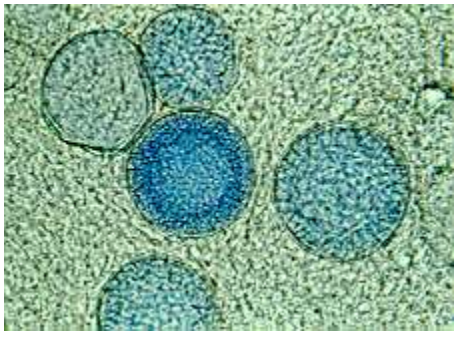
Chronic cutaneous coccidioidomycosis showing granulomatous lesions of the face, neck and chin .

Laboratory diagnosis:

1. Clinical material: Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, bone marrow, urine and tissue biopsies from various visceral organs.

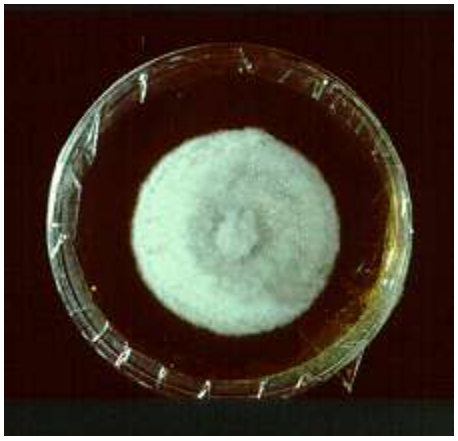
2. Direct Microscopy: (a) Skin scrapings should be examined using 10% KOH and Parker ink or calcofluor white mounts; (b) Exudates and body fluids should be centrifuged and the sediment examined using either 10% KOH and Parker ink or calcofluor white mounts, (c) Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

Histopathology is especially useful and is one of the most important ways of alerting the laboratory that they may be dealing with a potential pathogen.



Direct microscopy of skin scrapings from a cutaneous lesion mounted in 10% KOH and Parker ink solution showing characteristic endosporulating spherules (sporangia) of *Coccidioides immitis*. The presence of spherules with endospores is diagnostic..

3. Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood.



Culture of *Coccidioides immitis* showing a suede-like to downy, greyish white colony with a tan to brown reverse.

4. Serology: Immunodiffusion and/or complement fixation tests for the detection of antibody have proven to be useful in the diagnosis of Coccidioidomycosis especially in immunocompetent patients. However, detection of antibodies in immunosuppressed patients is often difficult, with between 20-50% of patients testing negative..

Causative agents: C*occidioides immitis*

Treatment

Less than 5% of infected, usually immunocompromised, humans develop a disease, and some mild asymptomatic cases often do not require any treatment. On the whole, oral fluconazole and intravenous amphotericin B are used in progressive or disseminated disease, or in which patients are immunocompromised . Fluconazole is preferred drug for coccidioidal meningitis, due to its penetration into CSF. amphotericin B therapy is used if infection persists after fluconazole treatment. Itraconazole is used for cases that involve treatment of infected patient's bones and joints.

Paracoccidioidomycosis (south American blastomycosis)

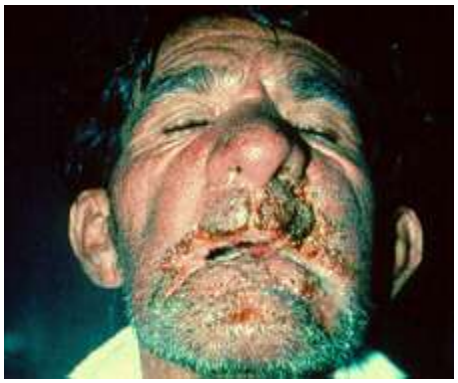
Paracoccidioidomycosis is a chronic granulomatous disease that characteristically produces a primary pulmonary infection, often in apparent, and then disseminates to form ulcerative granulomata of the buccal, nasal and occasionally the gastrointestinal mucosa. The disease in its inception and development is similar to blastomycosis and coccidioidomycosis. The only etiological agent, *Paracoccidioides*

brasiliensis is geographically restricted to areas of South and Central America.

Clinical manifestations:

Pulmonary paracoccidioidomycosis: Most cases have an indolent onset and patients present with chronic symptoms such as cough, fever, night sweats, malaise and weight loss. Chest x-rays are characteristic but not diagnostic. The infection must be distinguished from histoplasmosis and tuberculosis.

Mucocutaneous paracoccidioidomycosis: The mouth and nose are the most usual mucosal sites of infection. Painful ulcerated lesions develop on the gums, tongue, lips or palate and can progress over weeks or months. Perforation of the palate or nasal septum may occur. Cutaneous lesions often appear on the face around the mouth and nose, although patient with severe infection can have widespread lesions.



Mucocutaneous paracoccidioidomycosis showing extensive destruction of facial features..

Lymphonodular paracoccidioidomycosis: Lymphadenitis is common in younger patients. may progress to form abscesses with draining sinuses.

Disseminated paracoccidioidomycosis: Haematogenous spread of *P. brasiliensis* can result in widespread disseminated disease; including lesions of the small or large intestine, hepatic lesions, adrenal gland destruction, osteomyelitis, arthritis, and meningoencephalitis or focal cerebral lesions.

Laboratory diagnosis:

1. Clinical material: Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, bone marrow, and tissue biopsies from various visceral organs.

2. Direct Microscopy: (a) Skin scrapings should be examined using 10% KOH and Parker ink or calcofluor white mounts; (b) Exudates and body

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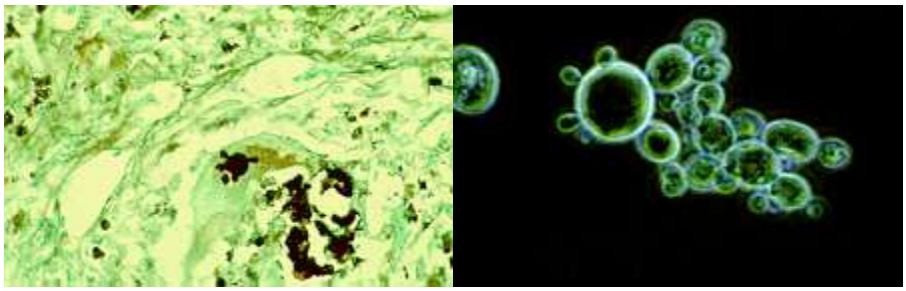

Multiple, narrow base, budding yeast cells "steering wheels" of *P. brasiliensis*. GMS stained lung section (left) and phase contrast of cells from a culture (right)..

3. Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood..

Causative agents: *Paracoccidioides brasiliensis*

Treatment

The most used sulfa drugs in this infection are sulfadimethoxime, sulfadiazine and co-trimoxazole. This treatment is generally safe but several adverse effects can appear, it must be continued for up to 3 years to eradicate the fungus.

Antifungal drugs like amphotericin B or itraconazole and ketoconazole are more effective in clearing the infection but limited by their cost when compared with sulfonamides. During therapy fibrosis can appear and surgery may be needed to correct this

Tissue morphology of dimorphic pathogens:

Mycosis	Tisue morphology
Blastomycosis	Large broad base unipolar budding yeast cells (8-10um).
Coccidioidomycosis	Spherules (10-80um) with endospores (2-5um).
Histoplasmosis	Small narrow base budding yeast cells (1-5um; 5-2um in var. duboisii)
Paracoccidioidomycosis	Large narrow base, multi-budding yeast cells (20-60um).
Sporotrichosis	Small narrow base budding yeast cells (2-5um).